

SHORT-TITLE: THEORY ON TIME REQUIRED FOR VACCINATION

**THEORETICAL FRAMEWORK AND EMPIRICAL MODELING FOR TIME REQUIRED TO
VACCINATE A POPULATION IN AN EPIDEMIC**

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ABSTRACT. The paper describes a method to understand time required to vaccinate against viruses in total as well as subpopulations. As a demonstration, a model based estimate for time required to vaccinate H1N1 in India, given its administrative difficulties is provided. We have proved novel theorems for the time functions defined in the paper. Such results are useful in planning for future epidemics. The number of days required to vaccinate entire high risk population in three subpopulations (villages, tehsils and towns) are noted to be 84, 89 and 88 respectively. There exists state wise disparities in the health infrastructure and capacities to deliver vaccines and hence national estimates need to be re-evaluated based on individual performances in the states.

Key words: Inequality theorems, population vaccination

1. INTRODUCTION

In recent years vaccination against influenza A (H1N1) has become one of the major concerns of health administrators around the globe. H1N1 has now returned to prominence following its recurrence in India and the news of 16 sudden deaths in the period between June and July, 2010 [1]. Progress in Indian vaccine research has raised the possibility of targeted or mass vaccination throughout India. Importantly, the mere availability of a vaccine does not immediately eliminate a pathogen from a population. Strategic planning covering vaccine production, distribution and, if necessary, importation will all be crucial components of a successful vaccination programme. India is a vast country with a massively variable health infrastructure distributed across Urban and Rural areas. Obtaining comprehensive vaccination coverage in some parts of India will be a challenging, but not impossible task. Recent precedents for the initiation of mass anti-flu vaccinations include Canada, whose government has decided to offer mass vaccination against H1N1 [2] and, previously, Israel who vaccinated its entire three million population against flu in 1988 [3]. Mathematical modeling can help to plan vaccine strategies and designs in the event of H1N1 [4]. Modeling can also help in understanding the impact of population coverage of H1N1 vaccines, impact in controlling due to delayed introduction of vaccines [5]. Mathematical analysis of the vaccination and elimination of disease from population has been well studied [6, 7, 8, 9, 10]. A completely new approach is introduced here in understanding the time required to vaccinate whole population and sub-populations. The concept of time required to vaccinate population and its sub-populations is addressed in the paper is explained in sections 2 and 3. As an example, we consider India and its states and divide these populations by three sub-types (Village, Tehsil, Town) based on administrative convenience. Although, a population can be divided into several other types of subpopulations viz., rural, urban or city, non-city urban, town, capitals etc, it is divided into above three types because administratively, such categorization helps in formal conceptualization of population vaccination schemes in India. In addition, our abstract framework proposed can be appropriately modified or expanded to suit several countries administrative structure. Consideration of the breadth and structure of the Indian population promotes the idea that vaccinating only high risk subpopulations may be more effective in a resource poor setting. Key questions associated with such large scale vaccination programmes include: what will be the time required to vaccinate four risk groups: pregnant women, children below five years of age, children aged 6 to 15 years of age and health professionals? Similarly, how long will be required to vaccinate the 1.20 billion population of India? In response to these questions, can we project a realistic timetable for effective vaccination using mathematical modeling to inform government decision making (given a formal starting date)? Answering these questions

will help in assessing the potential epidemic burden in the Indian population. The analysis described here will be true for any emerging epidemic in India.

This paper is divided mainly into empirical modeling and theoretical framework for understanding time required to vaccinate population in the event of an epidemic. The resulting framework leads to new results which provide bounds of *time functions* introduced to understand required time to cover the population after initiation of population vaccination programme. These mathematical results can be practically adoptable for visualizing strategies and their efficacy in the health systems in the populations.

2. EMPIRICAL MODEL

In this section we have computed time required to vaccinate high risk population by dividing total population into various strata and then carried out analysis through discrete computations.

Let $S_i (i = 1, 2, \dots, n_1)$, $T_j (j = 1, 2, \dots, n_2)$ and $U_k (k = 1, 2, \dots, n_3)$ be i th tehsil, j th town and k th village in the country. (Those who are not familiar with these type of administrative names, can think of three independent sub-populations. Entire population is distributed into these three sub-populations). Let $V_i(t)$ be the number of the vaccinated population per t units of time in some location l , α_i is the number of vaccine centers per each type of location, β_i is number of vaccinations given per hour in a vaccine center in each type of location, C_i is number of working hours for a vaccine center per day in each type of location, W_i is the number of working days per t units of time (Note : here t units are per week or per month).

We calculate $V_i(t)$ by $V_i(t) = \alpha_i \beta_i C_i W_i(t)$. Total population $P(t)$ is divided as $P(t) = p_A P(t) + p_B P(t)$, where p_A and p_B are the proportion of people in rural and urban areas. Let $P_{S_i}(t)$, $P_{T_j}(t)$, $P_{U_k}(t)$ be populations of i th tehsil, j th town and k th village respectively. Then the total tehsil, town and village populations are

$$(2.1) \quad \begin{aligned} P_S(t) &= \sum_{i=0}^{n_1} P_{S_i}(t) \\ P_T(t) &= \sum_{j=0}^{n_2} P_{T_j}(t) \\ P_U(t) &= \sum_{k=0}^{n_3} P_{U_k}(t) \end{aligned}$$

We compute $V_S(t)$, $V_T(t)$, $V_U(t)$ and then required time vaccination in the entire country by the type of location is $\frac{V_S(t)}{P_S(t)}$, $\frac{V_T(t)}{P_T(t)}$, $\frac{V_U(t)}{P_U(t)}$. In case the populations are very large, one can consider them as integral equations: $P_S(t) = \int_0^{n_1} P_{S_i}(t) di$, $P_T(t) = \int_0^{n_2} P_{T_j}(t) dj$, $P_U(t) = \int_0^{n_3} P_{U_k}(t) dk$. Let x_{ij} , y_{ik} , z_{il} be the times required to vaccinate in the i th state and j th village, i th state and k th tehsil, and i th state and l th town. We denote $\max_j(x_{ij})$, $\max_k(y_{ik})$, $\max_l(z_{il})$ for the corresponding maximum values of i th rows and $\min_j(x_{ij})$, $\min_k(y_{ik})$, $\min_l(z_{il})$ for the corresponding minimum values of i th rows in the following matrices X , Y , Z :

$$X = \begin{bmatrix} x_{11}, & x_{12}, & \dots, & x_{1V_1} \\ x_{21}, & x_{22}, & \dots, & x_{2V_2} \\ \vdots & \vdots & \vdots & \vdots \\ x_{S1}, & x_{S2}, & \dots, & x_{SV_S} \end{bmatrix}, Y = \begin{bmatrix} y_{11}, & y_{12}, & \dots, & y_{1H_1} \\ y_{21}, & y_{22}, & \dots, & y_{2H_2} \\ \vdots & \vdots & \vdots & \vdots \\ y_{S1}, & y_{S2}, & \dots, & y_{SH_S} \end{bmatrix},$$

$$(2.2) \quad Z = \begin{bmatrix} z_{11}, & z_{12}, & \dots, & z_{1T_1} \\ z_{21}, & z_{22}, & \dots, & z_{2T_2} \\ \vdots & \vdots & \vdots & \vdots \\ z_{S1}, & z_{S2}, & \dots, & z_{ST_S} \end{bmatrix}$$

We assume that vaccination will be introduced simultaneously in all three types of locations in each state. Then the time taken to completely vaccinate the general population in each state i is $\max \left\{ \max_j(x_{ij}), \max_k(y_{ik}), \max_l(z_{il}) \right\}$ for $j = 1, 2, \dots, V_i$; $k = 1, 2, \dots, H_k$; $l = 1, 2, \dots, T_l$.

Once we divide total centers in the country by the type of location in which they exist, then the total high risk population living in villages can be vaccinated within the time $\max_i \left\{ \max_j(x_{ij}) \right\}$ for $i = 1, 2, \dots, S$; $j = 1, 2, \dots, V_i$. Similarly, the total risk population living in tehsils and towns can be vaccinated within the time $\max_i \left\{ \max_k(y_{ik}) \right\}$ for $i = 1, 2, \dots, S$; $k = 1, 2, \dots, H_k$ and $\max_i \left\{ \max_l(z_{il}) \right\}$ for $i = 1, 2, \dots, S$; $l = 1, 2, \dots, T_i$.

In case the vaccinations are introduced to the risk population in the sequence of populations living in towns, tehsils, and villages in the state i , then within the days of $\max_i \left\{ \max_l(z_{il}) \right\}$ for $l = 1, 2, \dots, T_i$, $\max_i \left\{ \max_k(y_{ik}) \right\}$ for $k = 1, 2, \dots, H_i$, $\max_i \left\{ \max_j(x_{ij}) \right\}$ for $j = 1, 2, \dots, V_i$ the virus will spread to susceptible from infected individuals. Hence, simultaneous introduction could reduce the overall time required to vaccinate. This situation also impacts upon the development of herd immunity. Mathematical analysis can help us to understand the lower and upper limits of the time required to vaccinate in each state. If we denote R_i range of times for state i , then R_i can be computed as $[L_i, U_i]$, where

$$(2.3) \quad \begin{aligned} L_i &= \min_i \left\{ \min_j(x_{ij}), \min_k(y_{ik}), \min_l(z_{il}) \right\} \\ U_i &= \max_i \left\{ \max_j(x_{ij}), \max_k(y_{ik}), \max_l(z_{il}) \right\} \end{aligned}$$

The ranges of times taken for vaccinations in the towns and tehsils can be computed by $R_k = [L_k, U_k]$ and $R_k = [L_k, U_k]$, where $L_k = \min_i \left\{ \min_k(y_{ik}) \right\}$, $U_k = \max_i \left\{ \max_k(y_{ik}) \right\}$ and $L_l = \min_i \left\{ \min_l(z_{il}) \right\}$, $U_l = \max_i \left\{ \max_l(z_{il}) \right\}$.

The above analytical description is not dependent on the number of vaccine centers. We have provided arguments in this section for an arbitrary size of vaccine centers allocated in towns, tehsils and villages.

3. SPATIAL SPREAD THROUGH CONVOLUTION

We introduce three functions $\{D_i(X), D_j(Y), D_k(Z)\}$, which we call *time functions* for three type of populations that we are considering i.e. village, tehsil, and town in state i . These functions are defined as follows:

$$(3.1) \quad \begin{aligned} D_i(X) &= \max_j(x_{ij}) - x_{ij'} \\ D_i(Y) &= \max_k(y_{ik}) - y_{ik'} \\ D_i(Z) &= \max_l(z_{il}) - z_{il'} \end{aligned}$$

where $x_{ij'} = \min_i(x_{ij})$, $y_{ik'} = \min_i(y_{ik})$, $z_{il'} = \min_i(z_{il})$. Observe that $\{\min(x_{ij})\forall i\}$ is the set of minimum values of time taken to vaccinate villages in all the states and that $\{\max(x_{ij})\forall i\}$ is the set maximum values of time taken to vaccinate villages in all the states. Let μ be a measurable function describing the events $x_{ij'}, y_{ik'}, z_{il'}$ i.e. $\mu(x_{ij'})$, $\mu(y_{ik'})$, $\mu(z_{il'})$, are measurable function for the minimum times, let σ be the measurable function describing the time functions $\{D_i(X), D_j(Y), D_k(Z)\}$ defined as above. If we assume μ and σ are Lebesgue integrable on $(0, \infty)$, then convolution of μ and σ is

$$\mu * \sigma = \int_0^\infty \mu(t-w)\sigma(w)dw$$

We also know that when μ and σ are Lebesgue integrable on the entire realline and at least one of μ or σ is bounded on the real line, then

$$(3.2) \quad \mu * \sigma = \int_{-\infty}^\infty \mu(t-w)\sigma(w)dw$$

is bounded on the real line. Since the time taken to vaccinate is bounded as the epidemic will not be lasting more than a season, the property of convolution holds good. These kind of convolutions arise in several applied mathematics areas apart from well known results in pure mathematics (see [19, 20, 22]). For recent results applications of convolution approach see [22] and [23].

μ and σ provides us an estimate of density function of the maximum time taken to vaccinate in each state using convolution approach. Since μ and σ are Lebesgue integrable on $(0, \infty)$, it is well-known that $\mu, \sigma \in L^2(0, \infty)$ [here $L^2(a, b)$ is the set of all real valued measurable functions μ, σ on (a, b) such that μ^2, σ^2 are Lebesgue integrable on (a, b)]. We can verify that for any real numbers a_1 and a_2 , $a_1\mu + a_2\sigma$ is also in $L^2(0, \infty)$. Hence we can deduce $|(\mu, \sigma)| \leq \|\mu\| \|\sigma\|$, because inner product (μ, σ) is well defined by previous statement. From these arguments, we can state following theorem for the time functions.

Theorem 1. Suppose $\mu(x_{ij}), \mu(y_k), \mu(z_{il})$ are measurable functions of the times taken to vaccinate and $\sigma(D_i(X)), \sigma(D_i(Y)), \sigma(D_i(Z))$ are measurable functions of the time functions as defined in the section, then

$$i) \|\mu(x_{ij'}) + \sigma(D_i(X))\| \leq \|\mu(x_{ij'})\| + \|\sigma(D_i(X))\|$$

$$ii) \|\mu(y_{ik'}) + \sigma((D_i(Y)))\| \leq \|\mu(y_{ik'})\| + \|\sigma((D_i(Y)))\|$$

$$(3.3) \quad iii) \|\mu(z_{il'}) + \sigma((D_i(Z)))\| \leq \|\mu(z_{il'})\| + \|\sigma((D_i(Z)))\|$$

Proof. (i) follows by observing that,

$$\begin{aligned} & (\mu(x_{ij'}), \sigma((D_i(X)))) + 2(\mu(x_{ij'}), \sigma((D_i(X)))) + \\ & (\sigma((D_i(X))), \sigma((D_i(X)))) = \|\mu(x_{ij'})\|^2 + \|\sigma((D_i(X)))\|^2 + 2(\mu(x_{ij'}), \sigma((D_i(X)))) . \end{aligned}$$

We can prove (ii) and (iii) by a similar argument. \square

Theorem 2. If $\min_i(\cdot)$ and $\max_i(\cdot)$ are minimum and maximum values of the function ' \cdot ' over set of all populations $1 \leq i \leq S$, and $x_{ij'} = \min_i(x_{ij})$, $x_{ij*} = \max_i(x_{ij})$, then

$$(3.4) \quad \begin{aligned} (i) \max_i(D_i(X)) & \leq \left| \min_i(x_{ij'}) - \max_i(x_{ij*}) \right| \\ (ii) \min_i(D_i(X)) & \geq \left| \min_i(x_{ij*}) - \max_i(x_{ij'}) \right| \end{aligned}$$

holds good.

Proof. (i) Suppose $\max_i(D_i(X))$ attains for the state L for some $1 \leq L \leq S$. Let us denote this by $D_L(X)$. Recall that we have information on set of all the times taken for each sub-population within each state. Imagine for conceptual clarity that we have plotted these times for each subpopulation vertically on the y -axis corresponding to the states in the x -axis. Now, let the coordinate corresponding to L and at minimum of set of time values is denoted by $P = (L, x_{Lj'})$ on the plane. The corresponding co-ordinate on the set of maximum values obtained from each state is denoted by $Q = (L, x_{Lj*})$ on the plane. Note that $x_{ij'}$ is the minimum value and x_{ij*} is maximum value for the for state i .

Case I. Suppose $x_{Lj'} = \min_i(x_{ij'}) = x_{i'j'}$ and $x_{Lj*} = \max_i(x_{ij*}) = x_{i*j*}$, then

$$D_L(X) = \left| \min_i(x_{ij'}) - \max_i(x_{ij*}) \right|$$

Case II. Suppose $x_{Lj'} \neq \min_i(x_{ij'})$ and $x_{Lj*} = \max_i(x_{ij*}) = x_{i*j*}$, then obviously $x_{Lj'} > \min_i(x_{ij'}) = x_{i'j'}$. Denote $P' = (i', x_{i'j'})$. Let $(L, 0)$ and $(i', 0)$ be points on the x -axis corresponding to the states L and i' . Then, we have

$$(3.5) \quad \|(L, 0) - Q\| > \|(L, 0) - P\| > \|(i', 0) - P'\|$$

$$\implies |x_{Lj'} - x_{Lj*}| < |x_{i'j'} - x_{Lj*}|$$

$$(3.6) \quad \implies D_L(X) < \left| \min_i(x_{ij'}) - \max_i(x_{ij*}) \right|.$$

Case III. Suppose $x_{Lj'} = \min_i(x_{ij'}) = x_{i'j'}$ and $x_{Lj*} \neq \max_i(x_{ij*})$. We have, $x_{Lj*} < x_{i*j*}$. Denote $Q* = (i*, x_{i'j*})$. Since $(i*, 0)$ is a point on x -axis, it follows that $x_{i*j*} > x_{Lj*}$ and

$$(3.7) \quad \|(i*, 0) - Q'\| > \|(L, 0) - Q\|$$

$$\implies |x_{i*j*} - x_{Lj'}| > |x_{Lj*} - x_{Lj'}|$$

$$\implies D_L(X) < \left| \min_i(x_{ij'}) - \max_i(x_{ij*}) \right|.$$

Case IV. Suppose $x_{Lj'} \neq \min_i(x_{ij'}) = x_{i'j'}$ and $x_{Lj*} \neq \max_i(x_{ij*}) = x_{i*j*}$. Although $Q*$ is the point corresponding to $x_{i'j*}$ and $P' = (i', x_{i'j'})$ is the point corresponding to $x_{i'j'}$, we have,

$$\|P* - Q*\| < D_L(X)$$

and also,

$$\|P' - Q'\| < D_L(X)$$

Again,

$$(3.8) \quad \|(i*, 0) - Q*\| > \|(L, 0) - Q\|$$

and

$$\|(i', 0) - P'\| < \|(L, 0) - P\|$$

From these argument, we arrive at the following inequality,

$$D_L(X) < |x_{i'j'} - x_{i*j*}|$$

i.e. $D_L(X) < \left| \min_i(x_{ij'}) - \max_i(x_{ij*}) \right|$. Hence (i) is proved.

(ii) Suppose $\min_i(D_i(X))$ occurs for state ω for some $1 \leq \omega \leq S$. Let $D_\omega(X)$ be the corresponding value. Corresponding to $D_\omega(X)$, let us denote a point $U = (\omega, x_{\omega j'})$ on the set of values of minimum among X in each state. The corresponding point on the maximum values among X in each state is $V = (\omega, x_{\omega j*})$. Note that $x_{\omega j'}$ of U and $x_{\omega j*}$ of V need not be minimum among set of all the minimum values and maximum among set of all maximum values obtained for all the states. We will evaluate the situation in four following cases.

Case I. Suppose $x_{\omega j'} = \max_i(x_{ij'}) = x_{i*j'}$ and $x_{\omega j*} = \min_i(x_{ij*}) = x_{i'j*}$, then it is clear from previous type of agreement, that,

$$\begin{aligned}
D_\omega(X) &= |x_{i'j'} - x_{i*j'}| \\
(3.9) \qquad &= \left| \min_i(x_{ij*}) - \max_i(x_{ij'}) \right|
\end{aligned}$$

Case II. Suppose $x_{\omega j'} \neq \max_i(x_{ij'})$ and $x_{\omega j*} = \min_i(x_{ij*}) = x_{i'j*}$. Let $U' = (i*, x_{i'j*})$. Clearly, $x_{\omega j'} < x_{i*j*}$. We have,

$$\|U - V\| < \|(\omega, 0) - V\| \text{ and } \|(\omega, 0) - U\| < \|(i*, 0) - U'\|. \text{ Hence,}$$

$$\begin{aligned}
|x_{\omega j*} - x_{\omega j'}| &> |x_{\omega j*} - x_{i*j'}| \\
(3.10) \qquad \implies D_\omega(X) &> \left| \min_i(x_{ij*}) - \max_i(x_{ij'}) \right|
\end{aligned}$$

Case III. Suppose $x_{\omega j'} = \max_i(x_{ij'}) = x_{i*j'}$ and $x_{\omega j*} \neq \min_i(x_{ij*})$. The situation arises to $x_{\omega j*} > x_{i'j*}$. Let $V* = (i', x_{i'j*})$. The minimum value in the set of all maximum times occurs at the point $V*$. Clearly,

$$\|(i', 0) - V*\| < \|(\omega, 0) - V\| \text{ and } \|U - V\| < \|(\omega, 0) - V\|. \text{ Hence,}$$

$$\begin{aligned}
|x_{\omega j*} - x_{\omega j'}| &> |x_{i'j*} - x_{\omega j'}| \\
\implies D_\omega(X) &> \left| \min_i(x_{ij*}) - \max_i(x_{ij'}) \right|
\end{aligned}$$

Case IV. Suppose $x_{\omega j'} \neq \max_i(x_{ij'}) = x_{i*j'}$ and $x_{\omega j*} \neq \min_i(x_{ij*})$. We will have, $x_{\omega j'} < x_{i*j'}$ and $x_{\omega j*} > x_{i'j*}$. Let us assume $i*$ at point $V*$ is not equal to i' at U' . Observe that,

$$\|(i*, 0) - V*\| < \|(\omega, 0) - V\| \text{ and } \|(i', 0) - U'\| > \|(\omega, 0) - U\|. \text{ Hence,}$$

$$\begin{aligned}
|x_{\omega j'} - x_{\omega j*}| &> |x_{i'j*} - x_{\omega j'}| \\
\implies D_\omega(X) &> \left| \min_i(x_{ij*}) - \max_i(x_{ij'}) \right|
\end{aligned}$$

Alternatively, if we assume $i*$ at point $V*$ is equal to i' at U' , then the required results is straight forward. \square

Theorem 3. If $\min_i(.)$ and $\max_i(.)$ are minimum and maximum values of the function '.' over set of all populations $1 \leq i \leq S$, and $y_{ik'} = \min_i(y_{ik})$, $y_{ik*} = \max_i(y_{ik})$, then

$$\begin{aligned}
(i) \max_i (D_i(Y)) &\leq \left| \min_i (y_{ik'}) - \max_i (y_{ik*}) \right| \\
(ii) \min_i (D_i(Y)) &\geq \left| \min_i (y_{ik*}) - \max_i (y_{ik'}) \right|
\end{aligned}
\tag{3.11}$$

holds good.

Proof. It follows from the similar logic given in proof of the Theorem 2. We will consider the variables $D_i(Y)$, $D_L(Y)$ and $D_\omega(Y)$. \square

Theorem 4. If $\min_i(\cdot)$ and $\max_i(\cdot)$ are minimum and maximum values of the function ' \cdot ' over set of all populations $1 \leq i \leq S$, and $z_{il'} = \min_i(z_{il})$, $z_{il*} = \max_i(z_{il})$, then

$$\begin{aligned}
(i) \max_i (D_i(Z)) &\leq \left| \min_i (z_{il'}) - \max_i (z_{il*}) \right| \\
(ii) \min_i (D_i(Z)) &\geq \left| \min_i (z_{il*}) - \max_i (z_{il'}) \right|
\end{aligned}
\tag{3.12}$$

holds good.

Proof. It follows from the similar logic given in proof of the Theorem 2. We will consider the variables $D_i(Z)$, $D_L(Z)$ and $D_\omega(Z)$. \square

We will now explore relationship between *local time functions* and *global time functions* of vaccination. *Local time functions* we associate with subpopulations within a population and *global time functions* we associate with population itself. Define $\tilde{D}(i) = U_i - L_i$ for each i . Note, L_i must be equal to at least one of the values of x_{ij} , y_{ik} , z_{il} and U_i must be exactly equal to at least one of the values of x_{ij} , y_{ik} , z_{il} for $j = 1, 2, \dots, V_i$, $k = 1, 2, \dots, H_i$, $l = 1, 2, \dots, T_i$. From this definition, we can deduce following S number of inequalities:

$$\begin{aligned}
\{(x_{1j*} - x_{1j'}), (y_{1k*} - y_{1k'}), (z_{1l*} - z_{1l'})\} &\leq \tilde{D}(1) \\
\{(x_{2j*} - x_{2j'}), (y_{2k*} - y_{2k'}), (z_{2l*} - z_{2l'})\} &\leq \tilde{D}(2) \\
&\vdots \\
\{(x_{Sj*} - x_{Sj'}), (y_{Sk*} - y_{Sk'}), (z_{Sl*} - z_{Sl'})\} &\leq \tilde{D}(S)
\end{aligned}
\tag{3.13}$$

Theorem 5. Suppose $(x_{1j*} - x_{1j'}) \neq (y_{1k*} - y_{1k'}) \neq (z_{1l*} - z_{1l'})$. Then,

$$i) \tilde{D}(i) = (x_{1j*} - x_{1j'}) \quad \text{if, and only if,} \quad x_{ij*} = U_i \text{ and } x_{ij'} = L_i.$$

$$ii) \tilde{D}(i) = (y_{1k*} - y_{1k'}) \quad \text{if, and only if,} \quad y_{ik*} = U_i \text{ and } y_{ik'} = L_i.$$

$$iii) \tilde{D}(i) = (z_{1l*} - z_{1l'}) \quad \text{if, and only if,} \quad z_{il*} = U_i \text{ and } z_{il'} = L_i.$$

Proof. (i) Suppose $\tilde{D}(i) = (x_{1j*} - x_{1j'})$. This implies $U_i - L_i = (x_{1j*} - x_{1j'})$. Using the hypothesis and 3.13, we have $(y_{1k*} - y_{1k'}) < \tilde{D}(i)$ and $(z_{1l*} - z_{1l'}) < \tilde{D}(i)$. This implies $y_{ik*} < U_i$, $y_{ik'} > L_i$ and $z_{il*} < U_i$, $z_{il'} > L_i$. Hence, $x_{ij*} = U_i$ and $x_{ij'} = L_i$. Other part is straightforward. Similarly, we can prove (ii) and (iii). \square

4. RESULTS

We have demonstrated the idea of how to utilize the time function defined in section 3 both empirically (by applying on Indian data) and found bounds of these functions theoretically. The larger the time function for a population indicates the larger the duration to cover population in the same population. Once the vaccination is introduced in a sub-population (say, Z) then the value of time function would attain at most the absolute difference between z_{il*} and $z_{il'}$.

The size of the Indian population is expected to be 1.2 billion by the time of the 2011 census, distributed across 28 states and 7 union territories. Decentralizing the administration of vaccine kit distribution to 5767 tehsils, 7742 towns and 608786 villages by appointing nodal officers to each of these three sectors would reduce vaccination time. Population age, size and gender structure in each of these sectors are not uniform and they vary across the 640 districts within India [11]. If a vaccine center is set-up in every village then 358 million people can be vaccinated per week (assuming seven shots per hour in a twelve hour day, seven day working week). Importantly, it is clear that only a proportion of villages will be able to host a vaccination center. In India, approximately 888 million people live in villages, suggesting that it would take about 37 weeks (or 259 days) to vaccinate the entire rural population (assuming one in fifteen villages hosts a vaccine center, see Figure 1). Since the urban population is smaller than the rural population the number of vaccine centers required in the tehsil and town sectors will be much lower than will be required in villages. The installation of ten vaccine centers in each town and tehsil would allow 80 million people living in these areas to be vaccinated per week. At this rate it would take about four weeks (or 28 days) to vaccinate the entire urban population. Crucially, we estimate that 284.9 million people in villages and 100.1 million people in urban areas will fall into the combined risk group of children, pregnant women and health professionals. There were studies which found support to the model based idea of vaccinating high risk populations against H1N1 [5, 11]. We estimate that it will take about 11.9 weeks 12.69 weeks and 12.53 weeks to vaccinate the combined risk group in villages, tehsils and towns (Figure 1). Figures 2 and 3 illustrate the projected number of weeks required to vaccinate the entire population in rural and urban areas given a varying number of vaccination centers. We can also develop a mathematical model equivalent to these discrete computations. Should the provision and distribution of vaccine kits prove to be limiting then medium range predictions indicate that rural areas could be vaccinated within 18 weeks and urban areas within 20 weeks from a given start date assuming optimal vaccination center availability. The time taken to establish vaccination centers in rural and urban areas will become the limiting factor.

5. CONCLUSIONS

Both empirical and theoretical result presented in section 3 are novel and gave new insights to handle population vaccine programs. Recent precedents for large scale public health programmes in India include the introduction of hepatitis B vaccination in ten major states in 2008, where 50 % of the target population was vaccinated. Similarly, vaccination against Japanese Encephalitis, introduced in 2006, targeted 27 million children in 11 states and yielded almost 16 million immunizations [14]. Under

the universal immunization programme the government of India has prioritized vaccination against six diseases including tuberculosis. The highest coverage rate for BCG was reported in the third DLHS to be 86 % during 2007-2008 (District Level Health Survey). Nonetheless, the third round of the National Family Health Survey (NFHS-III) [15] indicated that immunization rates vary widely across the Indian states (Figure 4), influenced by variable vaccine procurement capacity and distribution. Based on these state-specific vaccine coverage rates the number of days likely to be required to vaccinate village, tehsil and town populations were adjusted (Figure 5). Identification of the underlying causes of these disparities in state-specific vaccination rates will require further research, taking into state infrastructure, health facilities, etc. See appendix for the impact of vaccination through the difference between two epidemic densities obtained from pre-vaccination era and post-vaccination era. Vaccine safety related issues also could lead to state level variations, for example studies conducted in elsewhere indicate distrust over H1N1 vaccines [16, 17, 18]. In order for these theoretical considerations to be achieved in practice it is essential that the government strengthens i) the rural health infrastructure, either empowering existing public health centers (PHCs) or setting-up new flu vaccine centers, ii) procurement and distribution of the required vaccines based upon size of the population, location etc. and iii) methods of identifying and reaching the high risk population in a timely manner.

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APPENDIX

We now use the framework of [24] for pre-vaccinated and post-vaccinated incidence densities. We assume that vaccination reduces the time to elimination of a pathogen from a population.

Let $\gamma_j (j = 1, 2, \dots, t_1)$ represent the peaks of infection densities in the year j . Suppose the number of years without introduction of the vaccination into the population is t_1 . Let $\gamma_K * (K = t_1 + 1, t_2 + 1, \dots)$ be the peaks of infection densities for the year K after introduction of the vaccines into the population. Let $m(j)$ and $m(k)$ be the means of incidence densities pre and post vaccinated populations, f_j and f_k be the corresponding density functions. Peak annual infection densities before vaccine introduction into the population is assumed to be higher than the peak of the corresponding densities after introduction of vaccination in the year $t_1 + 1$. Mean distance between peaks of incidence in j in $t_1 + 1$ is $d(\gamma_j, \gamma_{t_1+1})$ (say), then the mean $\bar{d}(\gamma_j, \gamma_{t_1+1})$ over all possible pre-vaccinated years is over all possible pre-vaccinated years is $\sum_j \frac{d(\gamma_j, \gamma_{t_1+1})}{t_1+1}$. (See [24]).

Table 1 : Parameters and description

Parameter	Description	Value	Reference or Source
p_A	Proportion of people living in rural India	26%	1, 6
p_B	Proportion of people living in urban India	74%	1, 6
n_1	Number of tehsils in the Country	5767	7
n_2	Number of towns considered to be in the Country	7742	7
n_3	Number of villages considered to be in the Country	600786	7
α_i	Number of vaccine centers by type of location	1 in 15 villages 1 in 1 town 1 in 1 tehsil	Assumptions
β_i	Number of vaccines given per hour by type of location	7 per 1 hour	Assumptions
C_i	Number of working hours by a vaccine center per day	8 hours in villages 12 hours in tehsils 12 hours in towns	Assumptions

